

## REMARKS

The Office Action, dated August 7, 2003, rejected claims 1 and 3-5. The claims were subject to a telephonic restriction requirement. Applicants herein affirm election of claims 1, 3, and 5, corresponding to the invention of Group I. Claim 4 has been withdrawn from consideration.

Upon entry of the present amendment, claims 1 and 4-12 are pending. In the present amendment, Applicants have canceled claim 3 without prejudice or disclaimer and amended claims 1 and 5. Applicants have also added new claims 6-14. The examination of claim 14, which depends from claim 7, would not pose a serious burden on the Examiner. See MPEP § 803 at 800-4 (8<sup>th</sup> ed., rev. 1). For example, a prior art search of claim 7, directed to a method of identifying gene regions that specify cell differentiation, would overlap substantially with a prior art search of claim 14, directed to the use of these gene regions to specify cell differentiation. Thus, Applicants respectfully request examination of new claims 6-14, along with elected claims 1 and 5.

Applicants have amended the claims and added new claims to further clarify the invention. The amendments and new claims are supported by the originally filed claims and the specification. Support for amended claims 1 and 5, directed to "obtaining a DNA methylation pattern," is found in the specification, for example, on page 5, lines 26-29 (last paragraph). Support for amended claim 5, directed to assessing a differentiation state, is found in the specification, for example, on page 9, lines 22-26 (last paragraph). Support for new claims 6 and 10, directed to DNA methylation patterns that "each comprise at least about 1,000 gene regions," is found in the specification, for example, at page 8, last line; page 19, line 3 (first full paragraph); and page 19, line 25 (Example 2). Support for new claims 7 and 11, directed to identifying

methyated and demethyated gene regions, is found in the specification, for example, at page 12, lines 17-23 (second paragraph under heading "2"), and page 19, lines 21-29 (Example 2). Support for new claims 8 and 12, reciting "a stem cell," is found in the specification, for example, on page 5, lines 13-14 (first full paragraph). Support for new claims 9 and 13, directed to RLGS profiles, is found in the specification, for example, on pages 6-10, and on page 3, lines 5-6 (describing Figure 3). Support for new claim 14, directed to producing a differentiated cell, tissue or nucleus, is found in the specification, for example, on page 12, line 30 (last line), through page 13, line 8. No new matter is added by these amendments and new claims.

**I. Rejection of Claim 5 Under 35 U.S.C. § 112, 2<sup>nd</sup> Paragraph (Indefinite)**

Claim 5 was rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to point out and distinctly claim the subject matter which Applicant regards as the invention. Claim 5, as amended, is clear and definite. Thus, Applicants respectfully request withdrawal of this rejection.

**II. Rejection of Claim 5 Under 35 U.S.C. § 112, 2<sup>nd</sup> Paragraph (Incomplete)**

Claim 5 was rejected under 35 U.S.C. § 112, second paragraph, as allegedly being incomplete for omitting an essential step, and in particular, for having a gap between steps. Without acquiescence and solely to facilitate prosecution, Applicants have amended claim 5, which recites completely the steps of the claimed method.

Thus, Applicants respectfully request withdrawal of this rejection.

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### III. Rejection of Claims 1, 3, and 5 Under 35 U.S.C. § 102(b)

Claims 1, 3, and 5 were rejected under 35 U.S.C. 102(b) as allegedly anticipated by U.S. Patent Number 5,871,917, issued February 16, 1999, to Duffy. Specifically, the Office Action states that:

Duffy shows in the abstract a method of comparison of DNA methylation patterns of cells. In some embodiments, the methylation pattern is at a coding or regulatory region of a gene. In some embodiments, the method is used as a diagnostic test to determine cancerous cell types. Duffy provides guidance in column 11 to use cancer cells, and to compare such cells with normal type cells from analogous tissues.

Office Action, page 4.

Claim 1 recites a method of identifying a cell, tissue or nucleus by obtaining comparing DNA methylation patterns. Duffy does not teach a method of identifying a cell, tissue, or nucleus by comparing DNA methylation patterns. Duffy teaches a subtractive hybridization method for isolating specific fragments of genomic DNA that are differentially methylated in cancerous or mutated cells. See, e.g., col. 2, lines 29-33. Duffy further teaches the use of such fragments as probes for detecting a potentially cancerous or mutant methylation state. *Id.* at col. 16, lines 30-34. Duffy does not teach a method comprising the step of "obtaining a DNA methylation pattern." Further, Duffy does not teach the step of "comparing the DNA methylation pattern[s] . . . thereby identifying a cell, tissue or nucleus," wherein regions of the genome with tissue- or cell-specific methylation provide the basis for identification. Thus, the method of Duffy is patentably distinct from the method of claim 1 as well as the method of claim 5, which recites analogous steps.

Duffy can be further distinguished from the present invention as follows. Duffy teaches a subtractive hybridization method wherein "tester" DNA is mixed with and

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hybridized to "driver" (control) DNA. See, e.g., cols. 15-16. Unhybridized tester DNA is then amplified, isolated, and used to detect differential methylation or mutation at only a few specific regions of the genome. *Id.* Duffy does not teach a method wherein the DNA methylation patterns of a first sample and a second sample are individually obtained and then compared. For example, the method of Duffy does not permit comparison of a tester DNA methylation pattern with a preexisting control DNA methylation pattern already stored in a database. (This example is provided solely to assist the examiner and should not be construed to so limit the present invention.) Duffy necessarily requires processing of the tester DNA in the presence of control DNA. Thus, the teachings of Duffy are patentably distinct from the invention of claims 1 and 5.

In view of the foregoing amendments and remarks, the rejection of claims 1 and 5 under 35 U.S.C. 102(b) is overcome. As claim 3 is canceled, the rejection is moot as to this claim. Withdrawal of this rejection is respectfully requested.

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### CONCLUSION

In view of the foregoing amendments and remarks, Applicants respectfully request reconsideration and reexamination of this application and the timely allowance of the pending claims. If the Examiner does not consider the application to be allowable, the undersigned requests that, prior to taking action, the Examiner call her at (650) 849-6778 to set up an interview.

Please grant any extensions of time required to enter this response and charge any additional required fees to our deposit account 06-0916.

Respectfully submitted,

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